Impact of Revised Stage Classification of Lung Cancer on Survival*

A Military Experience

Samuel A. Adebonojo, MD, FCCP; Andrew N. Bowser, MD; Dennis M. Moritz, MD; and Philip C. Corcoran, MD

**Study objectives:** This report reviews results of surgical management of lung cancer at a military medical center using the revised 1997 stage classification and determines the impact of the revised system on survival rates. It also compares our results with the recent reports from Japan and from a large, multinational study involving several institutions.

**Design:** Retrospective review.

**Setting:** Department of Cardiothoracic Surgery, Walter Reed Army Medical Center (WRAMC), Washington, DC.

**Patients or participants:** Active military members, their dependents, and eligible retired military members who were admitted to WRAMC for surgical treatment of lung cancer between January 1984 and December 1996.

**Methods:** Records of all patients who had surgical resection with intent to cure were reviewed. Data extracted included clinical and pathologic stages according to the 1997 revised stage classification. Survival probabilities for the stages were calculated by the Kaplan-Meier actuarial method. The log rank test was used to compare survival rates between stages and stage subsets. A p value $< 0.05$ was considered statistically significant.

**Measurements and results:** Five hundred fifty-two of the 1,398 patients with primary lung cancers underwent curative surgical resection (39.5%). The operative mortality was 2%. Using the revised 1997 stage classification, the survival rate for stage IA was 77%; IB, 62%; IIA, 57%; IIB, 47%; IIIA, 28%; IIIB, 20%; and IV, 0%. The overall actuarial 5-year and 10-year survival rates were 58% and 45%, respectively (median survival, 3.3 years; mean survival 3.9 ± 0.1 years).

**Conclusions:** Our results confirm the justification for the recent revisions in the staging system of lung cancer; however, there are still discrepancies that cannot be explained.

(CHEST 1999; 115:1507–1513)

**Key words:** lung cancer; lung cancer staging; lung neoplasm; surgery; survival rate

**Abbreviations:** AJCC = American Joint Committee on Cancer; UICC = International Union Against Cancer; WRAMC = Walter Reed Army Medical Center

*From the Veterans Affairs Medical Center (Dr. Adebonojo), and the Department of Surgery (Dr. Bowser), Wright State University School of Medicine, Dayton, OH; and the Department of Cardiothoracic Surgery (Drs. Moritz and Corcoran), Walter Reed Army Medical Center, Washington, DC.

The opinion and assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the Department of the Army, the Department of Veterans Affairs, or the Department of Defense.

Manuscript received September 25, 1998; revision accepted February 3, 1999.

Correspondence to: Samuel A. Adebonojo, MD, FCCP, Surgical Service, Veterans Affairs Medical Center, 4100 W Third Street, Dayton, OH 45428; e-mail: s.adebonojo@cwix.com

In 1946, Denoix introduced a system for the staging of lung cancer that was based on the estimation of the primary tumor (T), extent of involvement of locoregional lymph nodes (N), and presence or absence of distant metastasis (M). Unfortunately, no other system was found adequate until 4 decades later, when an international stage classification was developed by the American Joint Committee on Cancer (AJCC) in cooperation with the TNM Committee of the International Union Against Cancer (UICC), later reported by Mountain in 1986. This system remained the gold standard for lung cancer staging and was used worldwide for more than a decade. Several authors have since called attention to the wide variations in survival rates within the groups and noted the diversity and heterogeneity in the spectrum of disease stage. In

For related article see page 1494
Table 1—Revised (1997) TNM Stage Classifications for Lung Cancer*

<table>
<thead>
<tr>
<th>Stage</th>
<th>Classifications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occult</td>
<td>TXN0M0</td>
</tr>
<tr>
<td>Stage 0</td>
<td>TisN0M0</td>
</tr>
<tr>
<td>Stage IA</td>
<td>T1N0M0</td>
</tr>
<tr>
<td>Stage IB</td>
<td>T2N0M0</td>
</tr>
<tr>
<td>Stage IIA</td>
<td>T1N1M0</td>
</tr>
<tr>
<td>Stage IIB</td>
<td>T2N1M0</td>
</tr>
<tr>
<td>Stage IIIA</td>
<td>T3N1M0, T1N2M0, T2N2M0, T3N2M0</td>
</tr>
<tr>
<td>Stage IIIB</td>
<td>T4(any stage N)M0, (any stage T)N3M0</td>
</tr>
<tr>
<td>Stage IV</td>
<td>(Any stage T)(any stage N)M1</td>
</tr>
</tbody>
</table>

*Satellite tumor nodule(s) in ipsilateral primary tumor lobe(s) is designated T4. Separate tumor nodule(s) in ipsilateral nonprimary tumor lobe(s) is designated M1. Adapted from Mountain.5

1996, the AJCC and UICC adopted several revisions to the 1986 stage classification, which were later reported by Mountain in 1997 (Table 1).5 Mountain and Dresler6 have also resolved the inconsistencies in mediastinal lymph node stations classification as they relate to staging.

The purpose of this retrospective study is to review the survival characteristics of patients who underwent curative resection for lung cancer in a unique population of active duty military members, their dependents, and retired military members. The study also assesses the validity of the 1997 staging system. Our data included patients who underwent surgical resection with intent to cure using a staging system based on the pathologic examination of surgical specimens and lymph nodes and on the determination of the presence or absence of distant metastasis. Inoue and associates7 recently reported a series of 1,310 patients from three Japanese institutions using the new stage classification. To our knowledge, ours is the first report from the United States that attempts to evaluate the validity of the revised stage classification on the basis of the results of surgical outcome in patients from a large, single military institution.

Materials and Methods

Between January 1984 and December 1996, 1,398 patients were registered in the Lung Cancer Tumor Registry at Walter Reed Army Medical Center (WRAMC). The medical records of the 552 patients who underwent surgical resection with intent to cure were analyzed. All patients were operated on by residents under the supervision of staff thoracic surgeons. Thoracic lymphadenectomy was not routinely performed during this period of review, but mediastinal nodal sampling was obtained from at least four mediastinal nodal stations for pathologic staging. Data extracted from each patient's medical record included age, gender, race, smoking history, risk factors, comorbid diseases, tumor histology and location, adjuvant and induction therapies, date of last follow-up, operative complications, deaths from any cause, and the status of disease at the time of death. The follow-up period ranged from 1 to 12 years (median, 3.5 years; mean, 4.0 years).

Other relevant information was obtained during clinic visits and from hospital charts and telephone contact with patients or their relatives. Survival probabilities were calculated by the Kaplan-Meier actuarial method6 using a software package (Statistical Program for Social Sciences, 1994; SPSS Inc; Chicago, IL). The log rank test was used to compare survival probabilities between the stage subsets of the revised staging system. The survival rates for each stage were compared with recent reports based on the revised systems that were published by Mountain in 19975 and Inoue and associates in 1998.7 A p value < 0.05 was considered statistically significant.

Results

Description of Population

Of the 1,398 patients with primary lung cancer, 552 patients (39.5%) underwent surgical resection with intent to cure. There were 392 men (71%) and 160 women (29%), with ages ranging from 31 to 95 years old (median, 64 years old; mean (± SD), 63 ± 10 years old). Four hundred seventy-seven patients (86.4%) were white, 68 patients (12.3%) were African-American, and 7 patients (1.3%) were Asian. This is consonant with the ethnic composition of the US Army. Four hundred ninety-eight patients (90.2%) gave a smoking history of 50 to 80 pack-years, and 11 patients (2%) had a > 80 pack-year smoking history, whereas 415 patients (75.2%) were still smoking at the time of diagnosis. Two hundred forty-eight patients (44.9%) were hypertensive, 149 patients (26.9%) had COPD, and 133 patients (24.1%) had FEV₁ < 1.5 L. One hundred ten patients (19.8%) gave a history of coronary artery disease, and 84 patients (15.2%) had coronary artery bypass surgery within 3 months to 10 years before surgery for lung cancer.

Tumor Histologic Findings and Location

Of the 552 patients operated on for lung cancer, adenocarcinoma constituted 51.4%; squamous cell carcinoma, 37.3%; small cell lung cancer, 4.3%; bronchioloalveolar carcinoma, 3.4%; large cell carcinoma, 2.5%; and undifferentiated carcinoma, 0.9%. Thirty-six percent of the tumors were in the right upper lobe, 30% were in the left upper lobe, 14% were in the right lower lobe, 13% were in the left lower lobe, and 6% were in the middle lobe. Two thirds of the tumors were in the upper lobes.

Surgical Procedure and Adjuvant Therapies

Lobectomy was performed in 424 patients (76.8%), pneumonectomy in 71 patients (12.8%),...
and wedge or segmental resection in 57 patients (10.3%). Nineteen of the 342 patients (5.5%) with stages IA and IB received postoperative chemotherapy (mostly patients with small cell lung cancer), whereas 21 patients (6.1%) received postoperative radiation therapy. Forty-two of the 109 patients (38.5%) with stages IIA and IIB also received postoperative chemotherapy, whereas 21 patients (6.1%) received postoperative radiation therapy. Forty-two of the 109 patients (38.5%) with stages IIA and IIB also received postoperative chemotherapy, whereas 21 patients (6.1%) received postoperative radiation therapy. Forty-two of the 109 patients (38.5%) with stages IIA and IIB also received postoperative chemotherapy, whereas 21 patients (6.1%) received postoperative radiation therapy. 

Before 1990, a less standardized approach was used as adjuvant therapy for locally advanced (stages IIIA and IIIB) disease. Cisplatin, in combination with other agents given in two to three cycles, or radiotherapy to a total dose of 60 Gy was used according to institution protocol in use at the time of treatment. However, a more standardized approach has evolved since 1990. This standardized approach involved both chemotherapy and radiotherapy. The agents most commonly used were cisplatin and vinblastine followed by radiation therapy to a total dose of 60 Gy. More recently, concomitant radiotherapy with chemotherapy (carboplatin and paclitaxel) has been used. Ongoing studies are addressing the sequencing of these modalities to determine the optimal effectiveness.

**Survival Results**

Eleven of the 552 patients died during the perioperative period for an overall operative mortality of 2%. One of the 57 patients (1.7%) who had limited resection died, 5 of the 424 patients (1.2%) who had lobectomy died, and 5 of the 71 patients (7%) who had pneumonectomy died. Major complications included persistent air leak that lasted > 7 days in 44 patients (8%), cardiac arrhythmia in 42 patients (7.6%), and various space problems that required additional tube drainage in 17 patients (3%). Other minor complications included atelectasis that required bronchoscopy in 15 patients (2.7%), ARDS in 11 patients (2%), reoperation for bleeding in 3 patients (0.54%), postpneumonectomy empyema with bronchopleural fistula in 3 patients (0.54%), and congestive heart failure and acute myocardial infarction in 2 patients (0.36%).

Table 2 is a summary of the actuarial 5-year and 10-year survival rates (with median and mean [± SD] survival in years) of all patients by gender, race, and histologic findings. The overall actuarial 5-year and 10-year survival rates were 58% and 45%, respectively, with median survival of 3.3 years and mean of 3.9 ± 0.1 years (Fig 1). Table 3 shows the actuarial 5-year survival rates on the basis of the revised stage classification. There is a significant difference between the actuarial 5-year survival for stage IA (77%; median, 8 years; mean, 8.75 ± 0.3 years) and those of stage IB (62%; median, 7.6 years; mean, 7.8 ± 0.4 years; p = 0.006) (Fig 2). The actuarial 5-year survival for stage IIA was 57% (median, 5.4 years; mean, 5.0 ± 0.6 years), compared with
48% (median, 4.7 years; mean, 6.1 ± 0.6 years; p = 0.96) for stage IIB. The actuarial 5-year survival for stage IIIA was 29% (median, 2.4 years; mean, 3.6 ± 0.4 years), stage IIIB was 20% (median, 2.1 years; mean, 2.5 ± 0.7 years), and stage IV was 0% (median, 1.2 years; mean, 1.8 ± 0.5 years). Table 4 shows the comparison of the actuarial 5-year survival rates of pathologic stages I to IIIA between Mountain’s multinational series,5 the Japanese series,7 and the WRAMC series. There are striking similarities in the survival rates of these three series.

Figure 1 shows the survival curve for the 552 patients. Figure 2 shows the survival curves for stages IA and IB subsets, and Figure 3 shows the survival curves of stage IIB subsets. Although there is a 9% survival advantage between stages IIA and IIB (57% and 48%, respectively; p = 0.96), this is not statistically significant because of the small number of patients with stage IIA disease. However, the survival curve of T2N1M0 patients (48%; median, 4.8 years; mean, 5.8 ± 0.6 years) is almost superimposed on that of T3N0M0 patients (47%; median, 4.6 years; mean, 5.9 ± 0.7 years). Thirty-three of the 42 patients (78.6%) with T3N0 tumors each had chest-wall invasion that required en bloc resection with reconstruction but without adjuvant therapy, with a median survival of 3.9 years and a mean survival of 4.0 ± 0.6 years (95% confidence interval, 2.8 to 5.2 years). Five patients with T3N0 Pancoast’s tumors had induction radiotherapy, with a median survival of 3.5 years and a mean survival of 3.6 ± 0.7 years (95% confidence interval, 2.2 to 5.0 years).

Four patients with T3N0 tumors invading the diaphragm (in three patients) and the pericardium (in one patient) each had en bloc resection with primary closure of the diaphragm and patch closure of the pericardium without adjuvant therapy; all died within 16 months with a median survival of 15 months (mean, 14.3 ± 1.7 months). Figure 4 shows the survival curves of all the stage groupings on the basis of the revised stage classification. Figure 5 shows the survival curves on the basis of the status of lymph nodes found at surgery and from surgical specimens. Patients with negative nodes (N0) had better 5-year survival (66%) than did patients with positive N1 nodes (46%; p = 0.002) and patients with positive N2 nodes (25%; p < 0.001). Our findings are similar to those of Mountain and Dresler,6 who reported 5-year survival rates of 62%, 42%, and 25% for N0, N1, and N2 diseases, respectively.

**Discussion**

The past few years have brought significant changes to the classification and staging of lung cancer. These changes became necessary as a result of the heterogeneity of end results existing from the TNM categories within stage groups and of the need for greater specificity in stage classification. In 1996, the AJCC and UICC adopted several revisions to the 1986 stage classification, changes that were later published by Mountain in 1997 (Table 1).5 Also, Mountain and Dresler6 have addressed the inconsistency in the mediastinal lymph node classification for accurate TNM staging. As a result of these changes, one of our patients with two separate nodules of squamous cell carcinoma in an ipsilateral primary
tumor lobe, which were previously classified in an earlier publication\(^9\) as synchronous multiple primary lung cancers, was restaged as T4.

Inoue and associates,\(^7\) in a report of 1,310 patients from three institutions in Japan, confirmed the validity of the revised stage classification by Mountain.\(^5\)

We have assessed the validity of these changes and compared our experience from a single, large military institution with Mountain’s multicenter, multinational series and the Japanese multicenter series. The unique system established in the military for medical care allows for excellent follow-up and close monitoring of all patients in the study. Our survival data also reveal close correlation with reported series\(^5,10–13\) from several large, civilian-based populations. The management of lung cancer remains surgical for stages I and II subsets and palliative with chemoradiotherapy for advanced disease. However, certain subsets of patients with stages IIIA and IIIB whose tumors initially appear as unresectable may become resectable after induction chemoradiotherapy.\(^13–16\)

Our data further support the revisions to the staging system of lung cancer. Mountain,\(^5\) Inoue and associates,\(^7\) and Drings and coworkers\(^10\) have noted differences in the survival rates among the various stages that are similar to our findings. However, we could not show any survival advantage that was statistically significant between stages IB and IIA.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Mountain Series†</th>
<th>Inoue Series‡</th>
<th>WRAMC Series§</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>511</td>
<td>480</td>
<td>196</td>
</tr>
<tr>
<td>IB</td>
<td>549</td>
<td>271</td>
<td>146</td>
</tr>
<tr>
<td>II A</td>
<td>76</td>
<td>57</td>
<td>17</td>
</tr>
<tr>
<td>II B</td>
<td>375</td>
<td>187</td>
<td>92</td>
</tr>
<tr>
<td>II B subset</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T2N1M0</td>
<td>288</td>
<td>141</td>
<td>50</td>
</tr>
<tr>
<td>T3N0M0</td>
<td>87</td>
<td>46</td>
<td>42</td>
</tr>
<tr>
<td>III A</td>
<td>399</td>
<td>291</td>
<td>83</td>
</tr>
<tr>
<td>III A subset</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T3N1M0</td>
<td>55</td>
<td>39</td>
<td>17</td>
</tr>
<tr>
<td>T1N2M0</td>
<td>65</td>
<td>65</td>
<td>16</td>
</tr>
<tr>
<td>T2N2M0</td>
<td>150</td>
<td>150</td>
<td>37</td>
</tr>
<tr>
<td>T3N2M0</td>
<td>37</td>
<td>37</td>
<td>13</td>
</tr>
</tbody>
</table>

*NA = not available.
†Multinational, multicenter series.\(^5\)
‡Japanese multicenter series.\(^7\)
§Current study series.

**Table 4—Comparison of Actuarial 5-Year Survival Rates**

![Figure 3](http://publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21920/)

**Figure 3.** Actuarial survival curves of stage II B subsets. The curve for T2N1M0 is almost superimposed on that of T3N0M0, confirming the justification for moving T3N0M0 from stage III A to II B.

![Figure 4](http://publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21920/)

**Figure 4.** Actuarial survival curves of all stages using the revised (1997) stage classification. There is a downward trend in the 5-year actuarial survival in all stages.
One possible explanation for this finding could be the relatively small number of patients with stage IIA tumors in many reported series (1.4% of Mountain’s series, 3.1% of the WRAMC series, and 4.4% of the series by Inoue and associates). Nonetheless, our findings correlate with other reports and validate the changes in the revised stage classification.

Despite the recent changes and advances, many areas for improvement exist. Although the survival rate for patients with T3N0M0 tumors appears favorable, we note that this survival advantage with T3N0M0 tumors is seen only in patients with tumors involving the chest wall and not with tumors involving the diaphragm or pericardium. Inoue and associates also noted similar findings. They reported 35% actuarial 5-year survival for patients with T3N0M0 and T3N1M0 tumors invading the parietal pleura, 26% for tumors invading the chest wall, and 0% 3-year survival for tumors invading the diaphragm. Weksler and associates found that 8 of the 4,668 patients (0.17%) who underwent exploration for resection of lung cancer at the Memorial Sloan-Kettering Cancer Center from 1974 to 1995 had tumors invading the diaphragm. Four patients had T3N0M0 tumors, and the remaining four patients had T3N2 tumors. The mean survival for patients with T3N0 was 52.8 weeks: one patient was alive after 69.4 months, and the other three patients died of unrelated causes. Our three patients with tumors invading the diaphragm survived for 14, 15, and 16 months. In contrast, the 33 patients with tumors invading the chest wall had a median survival of 3.9 years and a mean survival of 4.0 ± 0.4 years. Although this number is small for any meaningful deduction, it is possible that chest wall tumors should retain the T3 designation, whereas tumors invading the diaphragm and pericardium should be designated as T4. There is also a need to further investigate the survival characteristics of patients with T3NOM0 disease to determine whether there are indeed significant survival differences within this tumor subset.

The 20% actuarial 5-year survival rate in the six patients with stage IIIb disease was indeed unexpectedly high. All six patients had T4N0 and T4N1 disease: three patients had tumors invading the thoracic vertebra, two patients had tumors invading the pulmonary artery, and one patient had two separate tumor nodules in the ipsilateral primary tumor lobe. All of the patients were operated on with intent to cure. None of these six patients had involvement of contralateral mediastinal (N3) nodes.

(62% vs 57%; p = 0.32). One possible explanation for this finding could be the relatively small number of patients with stage IIA tumors in many reported series (1.4% of Mountain’s series, 3.1% of the WRAMC series, and 4.4% of the series by Inoue and associates). Nonetheless, our findings correlate with other reports and validate the changes in the revised stage classification.

Despite the recent changes and advances, many areas for improvement exist. Although the survival rate for patients with T3N0M0 tumors appears favorable, we note that this survival advantage with T3N0M0 tumors is seen only in patients with tumors involving the chest wall and not with tumors involving the diaphragm or pericardium. Inoue and associates also noted similar findings. They reported 35% actuarial 5-year survival for patients with T3N0M0 and T3N1M0 tumors invading the parietal pleura, 26% for tumors invading the chest wall, and 0% 3-year survival for tumors invading the diaphragm. Weksler and associates found that 8 of the 4,668 patients (0.17%) who underwent exploration for resection of lung cancer at the Memorial Sloan-Kettering Cancer Center from 1974 to 1995 had tumors invading the diaphragm. Four patients had T3N0M0 tumors, and the remaining four patients had T3N2 tumors. The mean survival for patients with T3N0 was 52.8 weeks: one patient was alive after 69.4 months, and the other three patients died of unrelated causes. Our three patients with tumors invading the diaphragm survived for 14, 15, and 16 months. In contrast, the 33 patients with tumors invading the chest wall had a median survival of 3.9 years and a mean survival of 4.0 ± 0.4 years. Although this number is small for

**Conclusion**

This study supports the recent changes in the staging system of lung cancer as reported by Mountain in 1997 and confirmed by Inoue and associates in 1998. Our survival rates are similar, particularly among patients with stages I to IIIA. It would appear that the survival rates for the various stages and substages are in flux, and there may be a need for future modifications as we gain more knowledge about the biological behavior of lung cancer. The recent proposal by Margolis for a simple numeric designation of the present 18 TNM groupings numbered from 0 to 17 would make the staging system easier to remember and less cumbersome for clinicians involved in the management of lung cancer.

ACKNOWLEDGMENTS: The authors express their sincere thanks to Ms. Gail Taylor for her valuable help in extracting the data from the WRAMC Tumor Registry and to Ms. Danielle Howard for her assistance with data entry. We are also deeply grateful to Mrs. Carie S. Lambert and Professor Olutawo Abimbola Abimbola for their editorial assistance in the preparation of this article.

**REFERENCES**


**Figure 5. Actuarial survival curves based on the nodal status of surgical-pathologic specimens.** There are significant differences between N0 and N1 (p = 0.002) and between N1 and N2 (p = 0.001). These findings correlate with the recent report by Mountain and Dresler.